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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,454	EYJOLFSSON, RENIR	
	Examiner	Art Unit	
	Andriae M. Holt	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/14/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action acknowledges the receipt of the Preliminary Amendments filed on January 14, 2003. Claims 1-9 and 11 are original. Claim 10 has been amended. Accordingly, claims 1-11 are being examined on the merits herein.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Regarding claim 11, the phrase "including" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. The term "including" is being regarded as synonymous to "such as and for example" See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al 4,743,450 in view of Daniel et al. WO99/62560.

The compound of formula 1 is the basic structure for an ACE Inhibitor, which is well known in the art, including the weight percentage ranges. Harris teaches the combination of formula 1, (col. 2, formula I, line 15-20), component b, an alkali or alkaline earth metal carbonate to be used as a stabilizer (col. 1, line 60 and col. 3, lines30-34), and saccharide compound used in the mixture (col. 1, line 61), the formulation by which the industry standard ace inhibitor, Accupril (Pfizer, Inc. and Warner Lambert, US Patent 4,743,450) is produced. Harris et al. does not specifically teach or make provision that the formulation does not contain a substantial amount of a saccharide compound. However, as defined in the specification of the instant application "a substantial amount of a saccharide compound" is any amount that would generally be considered to have a stabilizing effect on the active compound, such as more than about 10 wt % and more preferably including an amount which is more than about 5 wt% (page 3, lines 18-22). The wt % ranges for the provision of the instant invention are within the specification of Harris et al, 1% to about 90%, preferably about 10% to about 80% (col. 3, lines 56-58).

Harris et al. does not teach an insoluble alkaline-earth metal salt of hydrogen phosphate. Daniel et al., however, does teach a hydrolysis-minimizing agent suitable to retard hydrolysis in combination with an ACE inhibitor, which is susceptible to cyclization, hydrolysis, and/or discoloration, and (b) an effective

amount of magnesium oxide suitable to retard cyclization, hydrolysis, and/ or discoloration. Daniel et al. specifically sites as an example, dicalcium phosphate, a calcium mono hydrogen phosphate, that is insoluble in water (page 3, lines 20-24).

It would have been obvious to one skilled in the art at the time of the invention to have been motivated to combine the practices of the formulations of Harris et al. and Daniel et al. That is substituting the hydrolysis minimizing-agents, saccharides with an insoluble alkaline-earth metal salt of hydrogen phosphate. Each essentially performs the same function of retarding hydrolysis of an ACE inhibitor that is susceptible to hydrolysis. It has been discovered that useful, stable formulations can be produced using excipients comprising basic compounds as evidenced by the formulations produced by Harris et al. and Daniel et al. Each formulation using the basic compounds has been proven to be effective and efficacious ACE Inhibitors in reducing hypertension in patient populations. The use of these compounds in combination has proven to have greater storage stability and more suitable for use in drug combinations (Harris et al. col. 1 lines 36-38). The active ingredients or drugs contained therein are virtually preserved from cyclization and hydrolysis. In addition, the discoloration, which sometimes occurs when ACE inhibitors of this class are formulated and allowed to stand for significant periods of time, is minimized or eliminated completely (Harris et al col. 1, lines 27-33). It is well known in the art that it would be advantageous to manufacture stable ACE Inhibitor agents using basic

compounds because these compounds are more cost effective to make or purchase.

In reference to claim 2, Harris et al, teaches the use of an alkaline stabilizer included in Group I and II of the periodic table combined with an anionic salt, magnesium, calcium and sodium are the preferred earth metals. Magnesium is most preferred. Carbonates are the preferred anionic salt (col. 3, lines 30-39).

Harris et al. teaches claim 3 that the amount of alkaline earth metal carbonate is at least equal to the amount of the active compound of formula I, as evidenced by comparing example 1 of the instant invention (Specification, page 5, lines 5-15) and example 1 of Harris et al. (col. 4, lines 56-67).

Claims 4 and 10 are taught by both references. Daniels et al., page 6, line 15, teaches enalapril and quinapril or, their corresponding free acids or pharmaceutically acceptable acid addition or base salts thereof. Harris et al., col. 2 lines 32-34, teaches enalapril and quinapril, their free acids or pharmaceutically acceptable acid addition or base salt thereof. These ace inhibitors are well known in the art: They each have very similar properties, including the structure of Formula 1 in Harris et al. (col. 2, line 15, formula 1).

The weight ranges in claim 5 are taught by Harris et al. (col. 2, lines 38-40). The total weight ranges for the total composition is 1% to about 70 %, preferably from about 1% to about 25 %.

The weight ranges of claims 6 and 7 of the alkali or alkaline earth metal carbonate are taught by Harris et al. (col. 3, lines 40-44) as the quantity of stabilizer to be used will lie between about 1% and 90%, preferably about 10 %

to about 80 %, encompassing ranges specified in the claims of the instant invention.

As per claims 8 and 9, Daniels et al., teaches the use of hydrolysis minimizing agents, including dicalcium phosphate, which is a calcium mono hydrogen phosphate, which is insoluble in water. The quantity of the hydrolysis-minimizing agent should be about 10% to about 95% preferably about 50% to about 95%, and most preferably 70% to about 90% (page 9, lines 5-17).

The suitable categories of drugs that can be combined in the embodiment of claim 11 of the instant invention are well known and well used in the art as categories that can be combined with ACE inhibitors, particularly quinapril, to provide an effective and efficacious anti-hypertensive agent with additive effects. Harris et al. and Daniel et al. teach claim 11 (Harris et al., col. 2, lines 60-68 and col. 3, lines 1-10; Daniel et al., page 7, lines 11-26).

Conclusion

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571) 272-9328. The examiner can normally be reached on 9:00 am - 5:00 pm EST M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER